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09/308,109	06/02/99	NASMYTH	K 0652.1880000

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EXAMINER

LULF
ART UNIT PAPER NUMBER

1655
DATE MAILED:

07/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/308,109

Applicant(s)

NASMYTH ET AL.

Examiner

Frank W Lu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 11-13 is/are pending in the application.
- 4a) Of the above claim(s) 1-6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 45
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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DETAILED ACTION

Election/Restriction

1. Applicant's election of Group III, claims 11-13 in Paper No. 14 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. The examiner noticed that some references in the specification are not in the IDS. For example, Wilm *et al.*, Nature 379, 466, 1996 (see page 39 of the specification) is not in form 1449.

Drawings

3. The drawings correction submitted on February 22, 2001 have been approved by the examiner. However, formal corrections can be deferred until the application is allowed by the examiner.

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Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance on how to reconstitute a recombinant APC complex and use any kind of substrate in the claimed method. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether recombinant individual subunits can work together to form a functional APC complex (E3 complex) in *in vitro* (Page *et al.*, Annual Review of Biochemistry, 68, 583-609, 1999, see page

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586, second paragraph) and whether any kind of substrate that can be ubiquitinated by APC dependent degradation is involved in the initiation of a new cell cycle. For example, the degradation of Scc1p/Mad1p does not seem to be required for sister chromatid separation (see Page *et al.*, page 593, last paragraph), a critical step for the initiation of a new cell cycle.

The invention relates to a method for identifying substances that inhibit rapidly proliferating cells by interfering with the cell's entry into the subsequent cell cycle comprising recombinant APC. The specification only describes that the expression systems such as baculovirus and the yeast *Pichia pastoris* offers the possibility to simultaneous expression several subunits to generate active complex (see page 6). However, the specification does not provide a guidance how to reach this goal. Applicant may argue that the expression systems such as baculovirus and the yeast *Pichia pastoris* are well established protein expression systems and a lot of different proteins have been produced by these systems, and one of skill in the art will have no problem to make APC using the similar methods. Although the examiner agreed with applicant in general concept, this is not the case here. First, the precise number of APC subunits is still not known (Peter, Experimental Cell Biology, 248, 339-349, 1999, see page 341, right column). Second, as suggested by Page *et al.*, (see page 604, first paragraph), the sheering number of subunit required for APC activity, not to mention specificity factors and activating kinase, will make the *in vitro* reconstitution of APC activity from purified components a daunting work. Third, the examiner could not found a successful report in APC reconstitution during prior art search (including applicant's papers). With these unpredictable factors, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue

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experimentation is required to make the invention as it is claimed. See M.P.E.P. 706.03(n) and 706.03(z). These undue experimentation at least includes: (1) reconstitute a functional recombinant APC complex; and (2) test whether any kind of substrate that can be ubiquitinated by APC dependent degradation as described in claim 11 is involved in the initiation of a new cell cycle.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Not that claims 12 and 13 are dependent on claim 11.

Claim 11 is rejected as vague and indefinite because it is unclear what it intended. For example, how a method for identifying substances in the presence of that inhibit rapidly proliferating cells by interfering with the cell's entry into the subsequent cell cycle will work without including a positive or/and negative control?

Claim 11 is rejected as vague and indefinite over the phrase "recombinant APC" because it is unclear what it intended. For example, does this phrase mean or mean functional APC complex consisting all APC subunits or mean something else?

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Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kirschner et al., (US Patent No. 5,726,025) teach a method for identifying an inhibitor of ubiquitin-mediated proteolysis of a cell cycle regulatory protein comprising CDC 27 and CDC 16 (two components of APC).

8. No claim is allowed.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
July 10, 2001

S. Zylmer
STEPHEN L. ZYLMER
PATENT EXAMINER